

Appendix A: Text of the Claims as Amended in Submission Dated July 7, 2003

1-84 (Previously cancelled)

1 ~~85.~~ (Previously presented) An assay for determining the presence or amount of a free and complexed cardiac specific isoform of troponin in a patient sample, said assay comprising:

performing an immunoassay with an antibody which specifically binds said ⁽¹⁾free cardiac specific isoform of troponin, and which specifically binds said cardiac specific isoform of troponin in a ⁽²⁾binary complex comprising one other troponin component selected from the group consisting of troponin I, troponin C and troponin T, and which specifically binds said cardiac specific isoform of troponin in a ⁽³⁾ternary complex comprising two other troponin components selected from the group consisting of troponin I, troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific isoform of troponin, wherein said signal is at least a factor of two larger than a signal resulting from said antibody binding to an equal number of (i) free troponin components which are not said cardiac specific isoform of troponin; (ii) troponin complexes which do not comprise said cardiac specific isoform of troponin; or (iii) a combination of (i) and (ii), and wherein said signal is related to the presence or amount of said free and complexed cardiac specific isoform of troponin in said sample.

2 ~~86.~~ (Previously presented) An assay according to claim ~~85~~, wherein said patient sample is selected from the group consisting of a blood sample, a serum sample, and a plasma sample.

3 ~~87.~~ (Previously presented) An assay according to claim ~~85~~, wherein said signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific isoform of troponin is at least a factor of five greater than said signal resulting from said antibody binding to an equal number of (i) free troponin components which are not said cardiac specific isoform of troponin; (ii) troponin complexes which do not comprise said cardiac specific isoform of troponin; or (iii) a combination of (i) and (ii).

4 ~~88.~~ (Previously presented) An assay for determining the presence or amount of free and complexed cardiac specific isoforms of troponin in a patient sample, said assay comprising:

performing an immunoassay with an antibody which specifically binds to free cardiac specific troponin I and cardiac specific troponin T, and which specifically binds to cardiac specific troponin I and cardiac specific troponin T in a complex comprising at least one other troponin component selected from the group consisting of troponin I, troponin C and troponin T, and which specifically binds to cardiac specific troponin I and cardiac specific troponin T in a ternary complex comprising two other troponin components selected from the group consisting of troponin I, troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific isoforms of troponin, wherein said signal is at least a factor of two larger than a signal resulting from said antibody binding to an equal number of (i) free troponin components which are not said cardiac specific isoforms of troponin; (ii) troponin complexes which do not comprise said cardiac specific isoforms of troponin; or (iii) a combination of (i) and (ii), and wherein said signal is related to the presence or amount of said free and complexed cardiac specific isoforms of troponin in said sample.

5 ~~89.~~ (Previously presented) An assay according to claim ~~88~~⁴, wherein said patient sample is selected from the group consisting of a blood sample, a serum sample, and a plasma sample.

6 ~~90.~~ (Previously presented) An assay according to claim ~~88~~⁴, wherein said signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific isoforms of troponin is at least a factor of five greater than said signal resulting from said antibody binding to an equal number of (i) free troponin components which are not said cardiac specific isoforms of troponin; (ii) troponin complexes which do not comprise said cardiac specific isoforms of troponin; or (iii) a combination of (i) and (ii).

7 ~~91.~~ (Previously presented) An assay for determining the presence or amount of free and complexed cardiac specific troponin I in a patient sample, said assay comprising:

performing an immunoassay with an antibody which specifically binds to free cardiac specific troponin I, and which specifically binds to cardiac specific troponin I in a complex comprising at least one other troponin component selected from the group consisting of troponin C and troponin T, and which specifically binds to cardiac specific troponin I in a ternary complex comprising troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific troponin I, wherein said signal is at least a factor of two larger than a signal resulting from said antibody binding to an equal number of (i) free troponin components which are not said cardiac specific troponin I; (ii) troponin complexes which do not comprise said cardiac specific troponin I; or (iii) a combination of (i) and (ii), and wherein said detectable signal is related to the presence or amount of said free and complexed cardiac specific troponin I in said sample.

8 ~~92.~~ (Previously presented) An assay according to claim ~~91~~⁷, wherein said patient sample is selected from the group consisting of a blood sample, a serum sample, and a plasma sample.

9 ~~93.~~ (Previously presented) An assay according to claim ~~91~~⁷, wherein said signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific troponin I is at least a factor of five greater than said signal resulting from said antibody binding to an equal number of (i) free troponin components which are not said cardiac specific troponin I; (ii) troponin complexes which do not comprise said cardiac specific troponin I; or (iii) a combination of (i) and (ii).

10 ~~94.~~ (Previously presented) An assay for determining the presence or amount of free and complexed cardiac specific troponin T in a patient sample, said assay comprising:

performing an immunoassay with an antibody which specifically binds to free cardiac specific troponin T, and which specifically binds to cardiac specific troponin T in a complex comprising at least one other troponin component selected from the group consisting of troponin C and troponin I, and which specifically binds to cardiac specific troponin T in a ternary complex comprising troponin C and troponin I; and

detecting a signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific troponin T, wherein said signal is at least a factor of two larger than a signal resulting from said antibody binding to an equal number of (i) free troponin components which are not said cardiac specific troponin T; (ii) troponin complexes which do not comprise said cardiac specific troponin T; or (iii) a combination of (i) and (ii), and wherein said detectable signal is related to the presence or amount of said free and complexed cardiac specific troponin T in said sample.

11 ~~95.~~ (Previously presented) An assay according to claim ~~94~~¹⁰, wherein said patient sample is selected from the group consisting of a blood sample, a serum sample, and a plasma sample.

12 ~~96.~~ (Previously presented) An assay according to claim ~~94~~¹⁰, wherein said signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific troponin T is at least a factor of five greater than said signal resulting from said antibody binding to an equal number of (i) free troponin components which are not said cardiac specific troponin T; (ii) troponin complexes which do not comprise said cardiac specific troponin T; or (iii) a combination of (i) and (ii).

97-101 (Previously cancelled)

13 ~~102.~~ (Previously presented) An assay for determining the presence or amount of all free and complexed cardiac specific isoforms of troponin in a patient sample, said assay comprising:

performing an immunoassay with an antibody which specifically binds all free cardiac specific isoforms of troponin, and which specifically binds all cardiac specific isoforms of troponin in a complex comprising at least one other troponin component selected from the group consisting of troponin I, troponin C and troponin T, and which specifically binds all cardiac specific isoforms of troponin in a ternary complex comprising two other troponin components selected from the group consisting of troponin I, troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific isoforms of troponin, wherein said signal is related to the

presence or amount of all free and complexed cardiac specific isoforms of troponin in said sample.

¹³
~~14~~ ~~103~~. (Previously presented) An assay according to claim ~~102~~, wherein said patient sample is selected from the group consisting of a blood sample, a serum sample, and a plasma sample.

¹³
~~15~~ ~~104~~. (Previously presented) An assay according to claim ~~102~~, wherein said signal is approximately equal for equal amounts of all cardiac specific isoforms of troponin.

¹³
~~16~~ ~~105~~. (Previously presented) An assay according to claim ~~102~~, wherein said signal is within 20% for equal amounts of all cardiac specific isoforms of troponin.

¹³
~~17~~ ~~106~~. (Previously presented) An assay according to claim ~~102~~, wherein said signal is within a factor of 2 for equal amounts of all cardiac specific isoforms of troponin.

107-113 (Previously cancelled)

¹⁸
~~18~~ ~~114~~. (Previously added) An assay for determining the presence or amount of a free and complexed cardiac specific isoform of troponin in a patient sample, said assay comprising:

performing an immunoassay with an antibody which specifically binds said free cardiac specific isoform of troponin, and which specifically binds said cardiac specific isoform of troponin in a complex comprising at least one other troponin component selected from the group consisting of troponin I, troponin C and troponin T, and which specifically binds said cardiac specific isoform of troponin in a ternary complex comprising two other troponin components selected from the group consisting of troponin I, troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific isoform of troponin, wherein said signal is related to the presence or amount of said free and complexed cardiac specific isoforms of troponin in said sample.

¹⁸
~~19~~ ~~115~~. (Previously presented) An assay according to claim ~~114~~, wherein said patient sample is selected from the group consisting of a blood sample, a serum sample, and a plasma sample.

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20 ~~116~~. (Previously presented) An assay according to claim ~~114~~, wherein a signal detected from said immunoassay for an amount of said free cardiac specific isoform of troponin is approximately equal to a signal detected from said immunoassay for an equal amount of said complexed cardiac specific isoform of troponin.

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21 ~~117~~. (Previously presented) An assay according to claim ~~114~~, wherein a signal detected from said immunoassay for an amount of said free cardiac specific isoform of troponin is within 20% of a signal detected from said immunoassay for an equal amount of said complexed cardiac specific isoform of troponin.

18
22 ~~118~~. (Previously presented) An assay according to claim ~~114~~, wherein a signal detected from said immunoassay for an amount of said free cardiac specific isoform of troponin is within a factor of 2 of a signal detected from said immunoassay for an equal amount of said complexed cardiac specific isoform of troponin.

23 ~~119~~. (Previously amended) An assay for determining the presence or amount of free and complexed cardiac specific isoforms of troponin in a patient sample, said assay comprising:

performing an immunoassay with an antibody which specifically binds to free cardiac specific troponin I and free cardiac specific troponin T, and which specifically binds to cardiac specific troponin I and cardiac specific troponin T in a complex comprising at least one other troponin component selected from the group consisting of troponin I, troponin C and troponin T, and which specifically binds to cardiac specific troponin I and cardiac specific troponin T in a ternary complex comprising two other troponin components selected from the group consisting of troponin I, troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific isoforms of troponin, wherein said signal is related to the presence or amount of said free and complexed cardiac specific isoforms of troponin in said sample.

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24 ~~120~~. (Previously presented) An assay according to claim ~~119~~, wherein said patient sample is selected from the group consisting of a blood sample, a serum sample, and a plasma sample.

- 25 ~~121.~~ (Previously presented) An assay according to claim ~~119~~²³, wherein a signal detected from said immunoassay for an amount of said free cardiac specific isoforms of troponin is approximately equal to a signal detected from said immunoassay for an equal amount of said complexed cardiac specific isoforms of troponin.
- 26 ~~122.~~ (Previously presented) An assay according to claim ~~119~~²³, wherein a signal detected from said immunoassay for an amount of said free cardiac specific isoforms of troponin is within 20% of a signal detected from said immunoassay for an equal amount of said complexed cardiac specific isoforms of troponin.
- 27 ~~123.~~ (Previously presented) An assay according to claim ~~119~~²³, wherein a signal detected from said immunoassay for an amount of said free cardiac specific isoforms of troponin is within a factor of 2 of a signal detected from said immunoassay for an equal amount of said complexed cardiac specific isoforms of troponin.
- 28 ~~124.~~ (Previously presented) An assay for determining the presence or amount of free and complexed cardiac specific troponin I in a patient sample, said assay comprising:
- performing an immunoassay with an antibody which specifically binds to free cardiac specific troponin I, and which specifically binds to cardiac specific troponin I in a complex comprising at least one other troponin component selected from the group consisting of troponin C and troponin T, and which specifically binds to cardiac specific troponin I in a ternary complex comprising troponin C and troponin T; and
- detecting a signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific troponin I, wherein said signal is related to the presence or amount of said free and complexed cardiac specific troponin I in said sample.
- 29 ~~125.~~ (Previously presented) An assay according to claim ~~124~~²⁸, wherein said patient sample is selected from the group consisting of a blood sample, a serum sample, and a plasma sample.
- 30 ~~126.~~ (Previously presented) An assay according to claim ~~124~~²⁸, wherein a signal detected from said immunoassay for an amount of said free cardiac specific troponin I is approximately equal

to a signal detected from said immunoassay for an equal amount of said complexed cardiac specific troponin I.

31 ~~127~~²⁸. (Previously presented) An assay according to claim ~~124~~²⁸, wherein a signal detected from said immunoassay for an amount of said free cardiac specific troponin I is within 20% of a signal detected from said immunoassay for an equal amount of said complexed cardiac specific troponin I.

32 ~~128~~²⁸. (Previously presented) An assay according to claim ~~124~~²⁸, wherein a signal detected from said immunoassay for an amount of said free cardiac specific troponin I is within a factor of 2 of a signal detected from said immunoassay for an equal amount of said complexed cardiac specific troponin I.

33 ~~129~~. (Previously presented) An assay for determining the presence or amount of free and complexed cardiac specific troponin T in a patient sample, said assay comprising:

performing an immunoassay with an antibody which specifically binds to free cardiac specific troponin T, and which specifically binds to cardiac specific troponin T in a complex comprising at least one other troponin component selected from the group consisting of troponin I and troponin C, and which specifically binds to cardiac specific troponin I in a ternary complex comprising troponin I and troponin C; and

detecting a signal from said immunoassay resulting from said antibody binding said free and complexed cardiac specific troponin T, wherein said signal is related to the presence or amount of said free and complexed cardiac specific troponin T in said sample.

34 ~~130~~³³. (Previously presented) An assay according to claim ~~129~~³³, wherein said patient sample is selected from the group consisting of a blood sample a serum sample, and a plasma sample.

35 ~~131~~³³. (Previously presented) An assay according to claim ~~129~~³³, wherein a signal detected from said immunoassay for an amount of said free cardiac specific troponin T is approximately equal to a signal detected from said immunoassay for an equal amount of said complexed cardiac specific troponin T.

36 ~~132~~. (Previously presented) ³³ ~~129~~ An assay according to claim ~~129~~, wherein a signal detected from said immunoassay for an amount of said free cardiac specific troponin T is within 20% of a signal detected from said immunoassay for an equal amount of said complexed cardiac specific troponin T.

37 ~~135~~. (Previously presented) ³³ ~~129~~ An assay according to claim ~~129~~, wherein a signal detected from said immunoassay for an amount of said free cardiac specific troponin T is within a factor of 2 of a signal detected from said immunoassay for an equal amount of said complexed cardiac specific troponin T.

38 ~~134~~. (Presently Amended) An assay for determining the presence or amount of a free and complexed cardiac specific isoform of troponin in a patient sample, said assay comprising:

performing an immunoassay with ~~An assay according to claim 85, wherein said antibody~~ is an antibody cocktail which specifically binds said free cardiac specific isoform of troponin, and which specifically binds said cardiac specific isoform of troponin in a binary complex comprising one other troponin component selected from the group consisting of troponin I, troponin C and troponin T, and which specifically binds said cardiac specific isoform of troponin in a ternary complex comprising two other troponin components selected from the group consisting of troponin I, troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody cocktail binding said free and complexed cardiac specific isoform of troponin, wherein said signal is at least a factor of two larger than a signal resulting from said antibody binding to an equal number of (i) free troponin components which are not said cardiac specific isoform of troponin; (ii) troponin complexes which do not comprise said cardiac specific isoform of troponin; or (iii) a combination of (i) and (ii), and wherein said signal is related to the presence or amount of said free and complexed cardiac specific isoform of troponin in said sample.

39 ~~135~~. (Presently Amended) An assay for determining the presence or amount of free and complexed cardiac specific isoforms of troponin in a patient sample, said assay comprising:

performing an immunoassay with ~~An assay according to claim 88, wherein said antibody~~
is an antibody cocktail which specifically binds to free cardiac specific troponin I and cardiac
specific troponin T, and which specifically binds to cardiac specific troponin I and cardiac
specific troponin T in a complex comprising at least one other troponin component selected from
the group consisting of troponin I, troponin C and troponin T, and which specifically binds to
cardiac specific troponin I and cardiac specific troponin T in a ternary complex comprising two
other troponin components selected from the group consisting of troponin I, troponin C and
troponin T; and

detecting a signal from said immunoassay resulting from said antibody cocktail binding said free
and complexed cardiac specific isoforms of troponin, wherein said signal is at least a factor of
two larger than a signal resulting from said antibody binding to an equal number of (i) free
troponin components which are not said cardiac specific isoforms of troponin; (ii) troponin
complexes which do not comprise said cardiac specific isoforms of troponin; or (iii) a
combination of (i) and (ii), and wherein said signal is related to the presence or amount of said
free and complexed cardiac specific isoforms of troponin in said sample.

40 ~~136.~~ (Presently Amended) An assay for determining the presence or amount of free and
complexed cardiac specific troponin I in a patient sample, said assay comprising:

performing an immunoassay with ~~An assay according to claim 91, wherein said antibody~~
is an antibody cocktail which specifically binds to free cardiac specific troponin I, and which
specifically binds to cardiac specific troponin I in a complex comprising at least one other
troponin component selected from the group consisting of troponin C and troponin T, and which
specifically binds to cardiac specific troponin I in a ternary complex comprising troponin C and
troponin T; and

detecting a signal from said immunoassay resulting from said antibody cocktail binding said free
and complexed cardiac specific troponin I, wherein said signal is at least a factor of two larger
than a signal resulting from said antibody binding to an equal number of (i) free troponin
components which are not said cardiac specific troponin I; (ii) troponin complexes which do not
comprise said cardiac specific troponin I; or (iii) a combination of (i) and (ii), and wherein said

detectable signal is related to the presence or amount of said free and complexed cardiac specific troponin I in said sample.

41 137. (Presently Amended) An assay for determining the presence or amount of free and complexed cardiac specific troponin T in a patient sample, said assay comprising:

performing an immunoassay with ~~An assay according to claim 94;~~ wherein said antibody is an antibody cocktail which specifically binds to free cardiac specific troponin T, and which specifically binds to cardiac specific troponin T in a complex comprising at least one other troponin component selected from the group consisting of troponin C and troponin I, and which specifically binds to cardiac specific troponin T in a ternary complex comprising troponin C and troponin I; and

detecting a signal from said immunoassay resulting from said antibody cocktail binding said free and complexed cardiac specific troponin T, wherein said signal is at least a factor of two larger than a signal resulting from said antibody binding to an equal number of (i) free troponin components which are not said cardiac specific troponin T; (ii) troponin complexes which do not comprise said cardiac specific troponin T; or (iii) a combination of (i) and (ii), and wherein said detectable signal is related to the presence or amount of said free and complexed cardiac specific troponin T in said sample.

42 138. (Presently Amended) An assay for determining the presence or amount of all free and complexed cardiac specific isoforms of troponin in a patient sample, said assay comprising:

performing an immunoassay with ~~An assay according to claim 102;~~ wherein said antibody is an antibody cocktail which specifically binds all free cardiac specific isoforms of troponin, and which specifically binds all cardiac specific isoforms of troponin in a complex comprising at least one other troponin component selected from the group consisting of troponin I, troponin C and troponin T, and which specifically binds all cardiac specific isoforms of troponin in a ternary complex comprising two other troponin components selected from the group consisting of troponin I, troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody cocktail binding said free and complexed cardiac specific isoforms of troponin, wherein said signal is related to the presence or amount of all free and complexed cardiac specific isoforms of troponin in said sample.

43/ 139. (Presently Amended) An assay for determining the presence or amount of a free and complexed cardiac specific isoform of troponin in a patient sample, said assay comprising:

performing an immunoassay with ~~An assay according to claim 114, wherein said antibody is an antibody cocktail~~ which specifically binds said free cardiac specific isoform of troponin, and which specifically binds said cardiac specific isoform of troponin in a complex comprising at least one other troponin component selected from the group consisting of troponin I, troponin C and troponin T, and which specifically binds said cardiac specific isoform of troponin in a ternary complex comprising two other troponin components selected from the group consisting of troponin I, troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody cocktail binding said free and complexed cardiac specific isoform of troponin, wherein said signal is related to the presence or amount of said free and complexed cardiac specific isoforms of troponin in said sample.

44/ 140. (Presently Amended) An assay for determining the presence or amount of free and complexed cardiac specific isoforms of troponin in a patient sample, said assay comprising:

performing an immunoassay with ~~An assay according to claim 119, wherein said antibody is an antibody cocktail~~ which specifically binds to free cardiac specific troponin I and free cardiac specific troponin T, and which specifically binds to cardiac specific troponin I and cardiac specific troponin T in a complex comprising at least one other troponin component selected from the group consisting of troponin I, troponin C and troponin T, and which specifically binds to cardiac specific troponin I and cardiac specific troponin T in a ternary complex comprising two other troponin components selected from the group consisting of troponin I, troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody cocktail binding said free and complexed cardiac specific isoforms of troponin, wherein said signal is related to the presence or amount of said free and complexed cardiac specific isoforms of troponin in said sample.

45 ~~141~~. (Presently Amended) An assay for determining the presence or amount of free and complexed cardiac specific troponin I in a patient sample, said assay comprising:

performing an immunoassay with ~~An assay according to claim 124, wherein said antibody is an antibody cocktail~~ which specifically binds to free cardiac specific troponin I, and which specifically binds to cardiac specific troponin I in a complex comprising at least one other troponin component selected from the group consisting of troponin C and troponin T, and which specifically binds to cardiac specific troponin I in a ternary complex comprising troponin C and troponin T; and

detecting a signal from said immunoassay resulting from said antibody cocktail binding said free and complexed cardiac specific troponin I, wherein said signal is related to the presence or amount of said free and complexed cardiac specific troponin I in said sample.

46 ~~142~~. (Presently Amended) An assay for determining the presence or amount of free and complexed cardiac specific troponin T in a patient sample, said assay comprising:

performing an immunoassay with ~~An assay according to claim 129, wherein said antibody is an antibody cocktail~~ which specifically binds to free cardiac specific troponin T, and which specifically binds to cardiac specific troponin T in a complex comprising at least one other troponin component selected from the group consisting of troponin I and troponin C, and which specifically binds to cardiac specific troponin T in a ternary complex comprising troponin I and troponin C; and

detecting a signal from said immunoassay resulting from said antibody cocktail binding said free and complexed cardiac specific troponin T, wherein said signal is related to the presence or amount of said free and complexed cardiac specific troponin T in said sample.